REMARKS

Applicants have added new claims 25-41, which recite a "replication competent" retroviral vector. Support for claims 25-41 is found e.g., on page 3, last paragraph, page 10, first paragraph and the working examples.

Claims 1-3, 5-7, 9-12 and 17-20 stand rejected under § 103 for purportedly being unpatentable over Winkler et al. and ter Meulen et al. Applicants respectfully disagree.

References relied upon to support a rejection under 35 U.S.C. §103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public. *In re Brown* 141 USPQ 245, 249 (CCPA 1964). An invention is not "possessed" absent some known or obvious way to make it. *In re Hoeksema* 158 USPQ 596, 601 (CCPA 1968). The combination of Winkler et al. and ter Meulen et al. fail to place the claimed invention in the possession of the public.

The present invention provides, for the first time, retroviral vectors of a feline foamy virus. Although not all of Applicants' claims recite a fully infectious viral DNA, a fully infectious DNA is a necessary preliminary intermediate for all the claimed vectors. In order to generate Applicants' claimed vectors, it is absolutely necessary to obtain a fully infectious and replication competent feline foamy virus DNA, from which vector constructs can be derived by deletion and/or modification of parts of the DNA. As discussed below, Winkler and ter Meulin alone and in combination fail to teach or suggest how one of skill in the art could make a fully infectious and replication-competent DNA of a feline foamy virus and therefore by failing to teach a necessary pre-requisite, they fail to teach or suggest how to make the claimed vectors.

ter Meulen et al. teach <u>human</u> foamy virus vectors. In particular, ter Meulen et al. teach obtaining foamy virus vectors by deleting viral genes from

the infectious, replication-competent clone of the human Spumaretrovirus (HSRV) (see col. 2, lines 9-15; col. 1, lines 45-53; col. 7, line 66 to col. 8, line 38). Thus, ter Meulen et al. confirms that an infectious, replication-competent full-length clone of the wild-type virus is the required intermediate for making foamy virus vectors. However, ter Meulen et al. fail to teach how to make a fully infectious and replication-competent clone of the feline foamy virus. Winkler et al. do not overcome the deficiencies of ter Meulen et al.

While Winkler et al. teach the genome of feline foamy virus, Winkler et al. fail to teach how to make a fully infectious and replication competent clone of the feline foamy virus. The sequence information given in Winkler et al. is not sufficient to guide a person of ordinary skill in the art to make an infectious and replication competent recombinant feline foamy virus DNA.

First, Winkler et al. fails to teach or suggest how to clone an infectious and replication-competent feline foamy virus. As shown in Applicants' Example 1, the full-length infectious and replication-competent feline foamy virus clone could not be cloned directly from the sub-genomic clones disclosed by Winkler et al. Applicants had to employ several additional procedures to obtain the new fragments (clones 24/28, clone V, fragment of clones 5, 7 and 15), which were then ligated with one another to generate complete proviral DNA of the feline foamy virus (see specification page 11, 2nd paragraph to page 12, 1st paragraph of the specification). None of these clones are disclosed or suggested by Winkler et al. Thus, the information of Winkler et al. is not enabling without undue experimentation for making a full-length clone of the feline foamy virus.

Moreover, as Applicants disclosed on page 12, 2nd paragraph, full-length clones were propagation deficient, because they could not go through the whole viral life cycle after the first infection of cells resulting in a self-limiting replication of virions. Therefore, the feline foamy virus clones made from Winkler et al.'s sequence information were not fully functional and, thus, not suitable for a retroviral vector having gene transduction capacity. The full

infectivity and replication competence had been only rescued by a second cloning step providing authentic and fully functional Env sequences, which second cloning step was not suggested in the prior art (see page 12, 2nd paragraph).

Thus, the teachings of Winkler et al. and ter Meulen et al. alone and in combination fail to disclose or render obvious a method for making an infectious, fully replication competent DNA genome of the feline foamy virus. Therefore, a person of ordinary skill in the art would not have had a reasonable expectation of successfully making an infectious, fully replication competent virus without undue experimentation. Without such an infectious, fully replication competent virus, which is a requisite for generating the claimed vectors, one of skill in the art would also not have reasonably expected to generate Applicants' claimed vectors.

In sum, obviousness cannot be predicted on what was not known at the time the invention was made. At the time the application was filed, it was not known how to make a fully infectious and replication competent viral DNA genome. And, although not all of Applicants' claims comprise a fully infectious viral DNA, a fully infectious DNA is an absolutely necessary preliminary intermediate for all the claimed vectors. Therefore, the claimed vectors are not obvious in view of Winkler et al. and ter Meulen et al. due to the absence of an obvious process for making fully infectious viral DNA and thus the claimed vectors.

In view of the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §103 in view of Winkler et al. and ter Meullen et al.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #104042.B270022).

Respectfully submitted,

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